

Rotenone and Paraquat Linked to Parkinson's Disease

Human Exposure Study Supports Years of Animal Studies

A growing body of evidence suggests pesticides may play a role in Parkinson's disease (PD) in humans. Self-reported PD has been associated with lifetime use of pesticides, and animal studies have suggested that the pesticides paraquat and rotenone can cause oxidative stress and mitochondrial dysfunction, respectively—posited mechanisms of action in PD—as well as symptoms in rodents similar to human PD. Now, researchers have linked human exposure to paraquat and rotenone with PD [*EHP* 119(6):866–872; Tanner et al.]. Their study is the first analysis of pesticides classified by presumed mechanism of action rather than by intended use or chemical class.

The researchers assessed lifetime use of pesticides as reported by participants in the Agricultural Health Study, a prospective study of private pesticide applicators (mostly farmers) and their spouses in Iowa and North Carolina. In the nested case-control study, neurologists specializing in movement disorders identified 110 people with PD and 358 controls without who were frequency matched by age, sex, and state.

The researchers collected detailed information about use of 31 different pesticides as well as covariate information including lifelong smoking and family history of PD. Each pesticide was classified according to its mechanism of action as either an oxidative stressor

or a mitochondrial complex I inhibitor. For participants with PD, the researchers considered pesticide use that occurred before their PD diagnosis. For controls, they considered pesticide use that occurred before the median age of PD diagnosis for cases in the corresponding age-, sex-, and state-specific groups.

Among the mitochondrial complex I inhibitors studied, the researchers found the strongest association between PD and use of rotenone. Among oxidative stressors, they found the strongest association between PD and use of paraquat. Participants with PD were 2.5 times more likely than controls to have reported use of rotenone or paraquat.

The results may have far-reaching implications, considering the widespread use of these pesticides. Paraquat remains one of the most widely used herbicides worldwide, and rotenone was used ubiquitously before most uses were voluntarily stopped in the United States in 2007. Other agents associated with mitochondrial complex I inhibition, such as permethrin, remain in common use.

The authors point out several limitations of the study, including the fact that participants reported exposure to many pesticides, and effects of other agents can't be excluded. However, the associations between PD and paraquat and rotenone remained after adjustment for overall pesticide use. It also was impossible to measure pesticide exposure, only estimate it retrospectively. Future investigations of combinations of pesticides and of other mechanistic groups will be important, as will mechanistic studies that model exposure conditions similar to those occurring in humans.

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Olympic Win

Lower Estimated Cancer Risk with Air Pollution Controls during the 2008 Beijing Games

Polycyclic aromatic hydrocarbons (PAHs) sorbed to fine atmospheric particulate matter (PM_{2.5}) increase inhalation cancer risk in exposed populations. In China each year, an estimated 6.5 people per million develop lung cancer due to PAH inhalation. But stringent air pollution control measures instituted during the 2008 Olympic Games in Beijing, if sustained over a lifetime, could reduce residents' PAH-related inhalation cancer risk by nearly half [*EHP* 119(6):815–820; Jia et al.].

Coal combustion and motor vehicle emissions create severe air pollution in Beijing and other major Chinese cities. To improve air quality for the Olympic Games, factories in and around Beijing were moved or closed, vehicular traffic was restricted, and truck traffic was reduced during the period 20 July–20 September 2008. During the games themselves (8–24 August), even stricter controls were imposed.

PM_{2.5} samples were collected at a single representative location in Beijing, and associated concentrations of 17 PAHs were measured and compared for four periods: 1) 28 July–20 September versus 2) 21 September–7 October, and 3) 8–24 August versus 4) 28 July–7 August/25 August–7 October. To enable direct comparison of chemical risks, a benzo[*a*]pyrene equivalent (BaP_{eq}) concentration was estimated for each PAH by multiplying its concentration by its relative potency factor (RPF). Cancer risk was calculated using the BaP_{eq} values paired with previously established unit risk measures for cancer based on a lifetime (70 years) of BaP exposure at 1 µg/m³ air.

Individual BaP_{eq} concentrations were 22–78% lower in period 1 compared with period 2 (i.e., when any pollution controls were in place) and 32–72% lower in period 3 compared with period 4 (i.e., when the strictest controls were in place). Lifetime excess inhalation cancer cases estimated during the period when pollution was controlled ranged from 6.5 to 518 individuals per million compared with a range of 12.2–964 per million after pollution controls ceased—a 46% reduction.

PAHs from the U.S. Environmental Protection Agency's list of priority pollutants made up three of the four largest contributors to total carcinogenicity; however, high-molecular-weight PAHs—a highly carcinogenic group of chemicals that, as a class, haven't been extensively studied—contributed a considerable 23% of the cancer risk. These top four PAHs are primarily associated with PM_{2.5}, so reducing PM_{2.5} emissions would also reduce levels of these and other PAHs.

Limitations of the study include potential inaccuracies due to its point-estimate approach, which assumes additive cancer risk, and the RPF values, which were based on toxicologic studies with their own uncertainties. However, the study strongly supports the effectiveness of air pollution source control measures and also demonstrated the need to include high-molecular-weight PAHs in future studies.

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Early morning rush hour, Tiananmen Square, Beijing